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Human Infection with *Shewanella putrefaciens* and *S. algae*: Report of 16 Cases in Martinique and Review of the Literature

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Abstract. *Shewanella* spp. are saprophytic bacteria that are part of the marine microflora in warm climates and are rarely pathogenic. However, *Shewanella* spp. infections are being increasingly reported, and there has been no comprehensive review of the literature describing these infections. This article reports 16 cases of *Shewanella* spp. infections in Martinique since 1997 and reviews another 239 cases reported in the literature since 1973. Patients experienced soft tissue infections, ear infection, or abdominal and biliary tract infections. A skin or mucosal portal of entry was found for 53% of the patients and exposure to the marine environment was reported for 44%; 79% of patients had an underlying condition. Bacteriema were frequent (28%). Most (87%) patients recovered, although ear infections can become chronic. Death occurred in 13% of the patients. Most *Shewanella* spp. isolates are susceptible to cefotaxime (95%), piperacillin and tazobactam (98%), gentamicin (99%), and ciprofloxacin (94%).

INTRODUCTION

Shewanella spp. are Gram-negative bacteria widely distributed worldwide; they are saprophytes and rarely pathogenic.[1] Their natural habitats are all forms of water and soil, but they have also been isolated from diverse sources including dairy products, oil, and carcasses.[2] They belong to the microflora of the marine environment (with *Vibrio paraheamolyticus*, *Aeromonas hydrophila*, *Plesiomonas*, and various enteric bacteria). In Denmark, *Shewanella* spp. have been isolated from sea water at temperatures > 13°C.[3]

The bacterium was first isolated in 1931 from putrefied butter and was successively called *Achromobacter putrefaciens*, *Pseudomonas putrefaciens*, *Alteromonas putrefaciens*, and finally *Shewanella* spp., of which 30 species have now been identifed.[4] The only species that have been isolated from clinical specimens are *S. putrefaciens* and *S. algae.* Important differential characteristics between the two species include the ability of *S. algae* to produce mucoid colonies with beta-hemolysis on sheep blood agar, grow at 42°C and in 6% NaCl (w/v), reduce nitrite, and an inability to produce acid from maltose, all of which are in contrast to the characteristics of *S. putrefaciens*.[5]

The pathogenicity of these species remains unclear, partly because they are found in polymicrobial infections, but there is now enough evidence to conclude that some *Shewanella* spp. are pathogenic for humans.[6] Most cases have been reported from areas with warm climates. *Shewanella* infections are sometimes acquired after exposure to seawater. The most common clinical manifestations seem to be otitis, soft tissue infection,[7] bacteremia, and hepatobiliary infection. Some argue than *S. algae* could be more virulent species.[2] *Shewanella* spp. have in rare cases been found associated with medical devices and can lead to health–care-associated infections and outbreaks.[8]

Infections with *Shewanella* spp. are rare, and there have been no systematic studies. Therefore, we report a review of *Shewanella* spp. infections reported to our Caribbean reference center and of other cases and series reported in the literature.

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PATIENTS AND METHODS

We reviewed all cases over a 14-year period, for which cultures were positive for *Shewanella* spp. in the Bacteriology laboratory of the University Hospital of Fort-de-France in Martinique. Patient files for 1997–2010 were reviewed retrospectively and those for 2011–2012 were included prospectively. Medical records were analyzed by physicians specialized in infectious disease from our university hospital. *Shewanella* spp. were cultured on Uriselect® medium (Biorad Laboratories, Hercules, CA) and identified by using the API® 20NE standardized system (Biomérieux, Marcy l'Etoile, France).

We searched for articles reporting cases of *Shewanella* spp infections in the PubMed database by using the following terms: *Achromobacter putrefaciens, Pseudomonas putrefaciens*, *Alteromonas putrefaciens*, *Shewanella*, *Shewanella putrefaciens*, *Shewanella alga*, and *Shewanella algae*. We included series and case reports. No prevalence or incidence studies were found. Standardized environmental, clinical, and bacteriologic data were collected and entered into a database. Data for patients from Martinique were added to the global case report database. Thus, global analysis includes all cases from Martinique, case reports, and series. Not all relevant data were available for each case, and consequently the number of observations is systematically specified in the results section. Stata version 10 (StataCorp LP, College Station, TX) was used for statistical analyses.

RESULTS

Martinique. In Martinique, we found 21 *Shewanella* spp.-positive clinical specimens isolated from 21 patients (7 women, 13 men, and 1 newborn). Their mean age was 61 years. The specimens were blood (3 specimens), pus (12), joint fluid (1), leg surgical site (1), bronchial aspiration (2), and gastric liquid (1). Five isolates were likely not pathogenic after review of patient file (specimens from skin, ulcer, or lung without clinical arguments for infection; one grows from joint fluid in only one specimen and other specimens remained negative). Sixteen of the 21 isolates were considered to be pathogens.

The clinical characteristics of these cases are summarized in Table 1. Half (8 of 16) of the infections were polymicrobial, and most often involved marine or gastrointestinal flora.

TABLE 1
Clinical characteristics of 16 patients with *Shewanella* spp. infection isolated in Martinique, 1997–2012

Year	Age, years	Sex	Underlying condition	Portal of entry	Type of infection	Bacteremia	Outcome	Co-isolates
1998	84	M	Prostatic cancer, venous insufficiency	Leg ulcer	Cellulitis	No		*Citrobacter freundii* and *Aeromonas sobria*
1998	27	M	No	Open fracture	Superinfection of open fracture with arthritis	No		Monomicrobial
1999	35	M	No	Open fracture	Superinfection of finger open fracture with necrosis	No	Death	*Aeromonas hydrohila*, *Enterobacter Cloacae*, and *Streptococcus D*
1999	73	M	Diabetes, heart failure	Blister	Cellulitis and abscess	No		*Aeromonas sobria*, *Staphylococcus aureus*, and Group B *Streptococcus*
2000	78	M	No	Open fracture	Superinfection of finger open fracture	No		*Aeromonas hydrophila*, *Enterobacter cloacae*, and *Enterococcus faecalis*
2002	78	M	Arteritis	Blister	Superinfection of blister	No		*Escherichia coli*
2005	66	F	Diabetes, amputated foot, renal failure	Amputation	Osteitis and erysipelas	No	Death	Gram-negative and -positive rods
2006	76	M	Diabetes, obesity, heart and renal failure	Leg ulcer	Superinfection of ulcer	No		*Staphylococcus aureus*
2007	83	F	Hypertension	Leg ulcer	Cellulitis	Yes	Death	Monomicrobial
2008	85	M	Arthritis, heart failure, chronic bronchitis	Leg ulcer	Cellulitis and leg abscess	No		Monomicrobial
2008	< 1	F	Newborn	Birth	Neonatal respiratory distress	No		Monomicrobial
2009	89	F	Cecal tumor, heart failure, diverticulosis	Digestive	Stercoral peritonitis	No	Death unrelated	Monomicrobial
2010	39	M	Osteosynthesis	Wound	Late abscess on osteosynthesis	No		*Staphylococcus lugdenensis*
2011	76	F	Heart failure	Leg ulcer	Cellulitis	Yes		Monomicrobial
2011	79	M	No	Wound	Cellulitis	Yes		Monomicrobial
2012	63	M	Chronic respiratory failure	Lung	Pneumonia	No		Monomicrobial

Soft tissue infection was the most frequent clinical presentation (11 of 16) and in some cases was complicated with abscess (3), osteoarthritis (1), or bacteremia (3). Other infections included superinfection of an open fracture (3 of 16), peritonitis (1 of 16), pneumonia (1 of 16), and neonatal infection (1 of 16). Four patients died. Three died secondarily from the infection (skin and soft tissue infection with bacteremia in two patients and osteitis with renal failure in one patient). Among the 11 patients with skin and soft tissue infections, nine had underlying conditions. A portal of entry was found in most (9 of 11) patients: chronic venous ulcers (4), post-traumatic ulcers (2), or wounds (3). We found history of sea water exposure for three patients. All isolates were susceptible to ceftazidime, piperacillin, and ciprofloxacin. None were susceptible to fosfomycin, 4 of 8 to amoxicillin, 13 of 15 to cefotaxime, 15 of 15 to cotrimoxazole, and 15 of 15 to gentamicin.

Review of the literature. We identified 56 articles published on PubMed search during 1973–2011, which reported 239 cases of *Shewanella* spp. infection or colonization.[7–55] Including the cases in Martinique, we analyzed a total of 260 cases. Twenty reported cases and five cases from Martinique were likely colonization (25 of 244). The mean age of the patients was 50 years (range = 0–90 years, n = 154) and 49 (39%) of 127 patients were women. Some neonatal cases were reported (one study in South Africa and one case in Martinique)[28] but the elderly were overrepresented (Table 2). The origins of the cases are shown in Table 2. Series have been reported in some countries, and these countries were thus overrepresented: Denmark (76),[32] South Korea (33),[8] South Africa (28),[28] United States (26),[13,23,31] Taiwan (19),[31] Belgium (9),[14] and India (5).[53]

Eleven percent of patients were immunocompromised (Table 3) because of cancer with chemotherapy (15), steroid use (4), splenectomy (2), neutropenia (2), human immunodeficiency virus HIV infection (1), and immunosuppressive drugs (1). Two-thirds had other underlying conditions: chronic ear disease (55), biliary tract lithiasis (8), cirrhosis (6), or other hepatobilary disease (21), heart failure (15), venous incompetence (9), renal failure (7), hypertension (7), arterial insufficiency (6), diabetes (6), gut surgery (6), peritoneal dialysis (6), chronic obstructive pulmonary disease (3), and obesity (3).

A skin or mucosal portal of entry was found for 53% of the cases (Table 3). The portals of entry were chronic leg ulcers (31), burns (4), wounds (32), rupture of the tympanic membrane (52), near drowning (1), mechanical ventilation (1), and

TABLE 2

Characteristics of patients with *Shewanella* spp. infection (case report database)

Variable	No. positive/no. tested (%)
Age	
Premature	9/154 (6)
Neonate	8/154 (5)
Child	9/154 (6)
Adult	85/154 (55)
Senior (> 65 years of age)	43/154 (28)
Residence	
Europe (Belgium, Denmark, France, Italy, Spain, Great Britain)	98/242 (40)
Australia	4/242 (2)
Caribbean (Martinique)	20/242 (8)
Pacific area (Hawaii)	1/242 (< 1)
Asia (Turkey, Japan, Korea, Taiwan, India)	64/242 (26)
Africa (South Africa)	28/242 (12)
North America (United States, Mexico)	27/254 (11)

loco-regional tumor (1). Exposure to the marine environment was reported for 44% of the cases, for which relevant information was available (Table 3).

The clinical spectrum of the disease is shown in Table 4. Ear infections were the most commonly reported infections, particularly in the series in Denmark. There were 53 cases of otitis media, 1 case of with cerebral abscess, 15 cases of chronic otitis, and eight cases of otitis externa. Skin and soft tissue infections were common (27%), comprising 19 cases of cellulitis, 6 cases of abscesses, 1 case of empyema, 3 cases of necrotizing fasciitis, 1 case of tonsillitis, 1 case of extensive myonecrosis, 3 cases of infections or colonizations of an open fracture, 5 cases of colonizations or chronic infections of a non-healing ulcer, and 3 cases of non-healing wounds. Abdominal and biliary tract infections were also reported: 10 biliary tract infections, 2 with cholecystitis, five with peritonitis, 1 with abdominal wall abscess, and 1 with paracolic abscess. For these case-patients, the portal of entry was digestive. The last common type of infection was respiratory infection: 10 cases of pneumonia, 2 cases of acute exacerbations of COPD, 1 case of bronchitis, 2 cases of ventilator-associated pneumonia, 17 cases of neonatal respiratory distress, 1 case of pulmonary abscess, and 1 case of acute exacerbation of bronchiectasis. Other sporadic clinical presentations are shown in Table 4.

Bacteremia was the most common complication (71 of 256, 28%). It was associated with skin and soft tissue infection (23 of 71, 33%), abdominal or biliary tract infection (13 of 71, 19%), or respiratory infection (21 of 71, 30%). Bacteremia was not associated with ear infection in any case.

The infection was considered serious (hypotension, secondarily organ failure, or death) in 21% (50 of 242) of cases. Fifty (19%) of 259 cases were described as possible healthcare-associated infections. An outbreak of 31 abdominal and biliary tract infections, or bacteremia, caused by exposure to a shared measuring cup was reported in a general surgery unit in South Korea.[8] Other infections in this group were two cases of ventilator-associated pneumonia,[45,54] five cases of peritonitis in patients undergoing peritoneal dialysis,[26,27,31] eight cases of skin and soft tissue infections,[24,31] one case of keratitis,[49] one case of bacteremia caused by endoscopic therapy of gastric varices,[31] one case of meningitis after trepanation,[21] and one case of urinary tract infection associated with catheterization.[14]

TABLE 3

Condition and portal of entry of patients with *Shewanella* spp. infection (case report database)

Variable	No. positive/no. tested (%)
Condition	
None	45/216 (21)
Immunocompromised	24/216 (11)
Underlying condition	147/216 (68)
Portal of entry	
None	116/249 (47)
Skin or mucosal injury	133/249 (53)
Water exposure	
None	65/168 (42)
Salt water	67/168 (44)
Fresh water	36/168 (24)

TABLE 4

Clinical characteristics of patients with *Shewanella* spp. infection (case report database)

Type of infection*	No. positive (%)
Skin and soft tissue	70 (27)
Bacteremia	71 (28)
Abdominal or biliary tract	43 (17)
Respiratory	34 (13)
Ear	84 (33)
Other	17 (7)
Bone	2 (1)
Urinary tract	4/256 (2)
Eye infection	3/256 (1)
Endocarditis	1/256 (< 1)
Meningitis	1/256 (< 1)
Aneurysm infection	1/256 (< 1)
Cerebral abscess	2/256 (1)

*Some patients had more than one infection.

TABLE 5

Antibiotic susceptibility of clinical *Shewanella* spp. isolates (case report database)

Antibiotic	No. positive/no. tested (%)
Penicillin G	0/8 (0)
Amoxicillin	25/114 (22)
Amoxicillin/clavulanic acid	9/12 (75)
Cefazolin	5/15 (33)
Cefotaxime	128/135 (95)
Ceftriaxone	51/54 (94)
Ceftazidime	69/73 (95)
Cefepime	19/20 (95)
Ticarcillin	36/47 (77)
Ticarcillin/clavulanic acid	15/18 (83)
Piperacillin	51/54 (94)
Piperacillin/tazobactam	54/55 (98)
Imipenem	103/125 (82)
Gentamicin	144/146 (99)
Tobramycin	18/18 (100)
Netilmicin	14/14 (100)
Amikacin	76/76 (100)
Colistin	16/30 (53)
Trimethoprim/sulfamethoxazole	62/143 (43)
Ofloxacin	14/16 (88)
Ciprofloxacin	121/129 (94)
Fosfomycin	0/19 (0)
Erythromicin	91/94 (97)
Chloramphenicol	115/116 (99)
Tetracycline	104/117 (89)
Polymyxin B	5/73 (7)

Most (87%, 195 of 223) patients recovered, although some cases of ear infection became chronic. Death occurred in 26 (13%) of 208 case-patients. Death was related to the infection in 18 (86%) of 21 cases for which information was available.

Bacteria isolated were *Pseudomonas putrefaciens* (19%, 49 of 253), *Shewanella putrefaciens* (37%, 93 of 253), and *Shewanella algae* (44%, 112 of 253). However, 16S rRNA analysis was not performed systematically to confirm the identification.

Bacteria was isolated from pus (49%, 112 of 230), blood (30%, 69), bile (7%, 16), or other specimens (17%: ascitic fluid [7], peritoneal dialysate [5], bronchoalveolar lavage fluid [2], sputum [7], urine: $> 10^4$ bacteria/mL [4]), corneal stroma and vitreous fluid [2], feces [2], bone [1], disc biopsy specimen [1], cerebral abscess [1], pulmonary abscess [1], pleural effusion [1], neonatal gastric liquid and anus [1], bronchic aspiration [2], articular fluid [1], and tonsilar pus [1]). The culture was polymicrobial in 99 (53%) of 188 cases. Co-isolates were gram-negative rods in 64% and gram-positive cocci in 30%. Associated bacteria from marine flora were reported in some cases (*Aeromonas hydrophila* and *A. sobria* [8], *Vibrio alginolyticus* [3], *Vibrio vulnificans* [1], and *Mycobacterium marinum* [1]). Antibiotic susceptibility of *Shewanella* spp. isolates is shown in Table 5.

DISCUSSION

Shewanella spp. infections have been reported worldwide. The cases include soft tissue infections, ear infections, abdominal infections, and biliary tract infections. Infections involving these species are frequently associated with underlying conditions and complications.

Although we intended to provide a comprehensive overview of the state of the knowledge of *Shewanella* spp. infections, our review has several limitations. In particular, many of the cases are single-case reports or small series. Thus, reporting bias is plausible. Furthermore, all relevant information that could be expected was not available from all publications.

There is substantial heterogeneity between cases reports and series, and they do not appropriately reflect the distribution of *Shewanella* spp. infections worldwide. Other than small series reported in Taiwan,[31] South Africa,[28] and Belgium,[14] the healthcare-associated epidemic in South Korea,[8] a larger series of otitis cases in Denmark,[32] and our retrospective study in Martinique, there have been no epidemiologic studies, either retrospective or prospective. We therefore compiled case reports to generate a description of the clinical and bacteriologic spectrum of this infection. *Shewanella* spp. infection seems to be ubiquitous: it has been observed in temperate regions during summer but is more common in intertropical areas.

Most of the clinical isolates are *Shewanella putrefaciens*, but recent data suggest that many of these isolates should be classified as the genetically distinct species *Shewanella algae*.[5] Some argue that *S. algae* may be a more virulent species.[2] This misclassification is largely caused by the use of conventional systems that are unable to identify *S. algae* (API® 20 NE system, ID 32 GN, or VITEK® 2 GN; Biomérieux). Accurate bacteriologic identification requires the use of molecular typing (16S rRNA sequence analysis). In our 21 cases, we performed 16S rRNA only three times for the three most recent isolates initially identified as *S. putrefaciens* by biochemical methods. All three isolates were identified as *S. algae* by molecular analysis. As has been suggested elsewhere, some of the *S. putrefaciens* infections reported during recent years were probably caused by *S. algae*.[5]

The clinical spectrum of human *Shewanella* spp. infections is wide; otitis, skin and soft-tissue infection,[31] hepatobiliary infection, and peritonitis[32] are the most frequent. This spectrum is similar to those of infections involving other marine bacteria (*Aeromonas* spp., *Vibrio* spp.).[56] This bacterium can be involved in neonatal infections as shown by a study in South Africa (respiratory distress with bacteremia) and one case in Martinique.[28] Serious infections and bacteremia are common.[18,28] Chronic infection of the legs, liver disease, and neonatal infections have been identified as possible risk factors for bloodstream infection by *S. putrefaciens*.[18,23,28] The death rate is high, although this finding may be partially explained by the high frequency of underlying conditions and bacteremia.

Shewanella putrefaciens was often isolated from cases of polymicrobial infection. Most of the strains co-isolated from such polymicrobial infections were enterobacteriaceae, but bacteria of marine flora were also found.[31,36] This pattern of co-isolates is consistent with portals of entry (gastrointestinal in most cases) and environmental flora.

Our study confirms that exposure to the marine environment is a risk factor for *Shewanella* spp. infection. The frequency of skin disease among patients with chronic ulcers or breaks in the skin and hepatobiliary infections suggest that *Shewanella* spp. may also be a commensal of the skin and present in gastrointestinal flora. Chronic diseases facilitate the occurrence of infection. Patients with lower leg ulcers should be advised to avoid exposure to the marine environment.

Shewanella spp. can show resistance to penicillins initially used to treat soft tissue infection. However, treatment of *Shewanella* spp. infections is straightforward once the antibiogram is available. *Shewanella* spp. are susceptible to commonly used antimicrobial agents, particularly third-generation cephalosporins, piperacillin, ciprofloxacin, and gentamicin. Because *Shewanella* spp. are oxidase positive, laboratories tend to test broad-spectrum antibiotics. However, it may be of value to test narrow-spectrum antibiotics because many *Shewanella* spp. isolates are susceptible to amoxicillin and third-generation cephalosporins. It is important to note that *Shewanella* can show resistance to imipenem by secreting an oxacillinase.[57]

Infection with *Shewanella* spp. infections should be considered in a suggestive environmental context (tropical area, sea water exposure). The use of molecular typing should be encouraged when *Shewanella* spp. are isolated. Epidemiologic studies are required to confirm these observations.

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